

Remarks

Claims 1-16 are pending in the application. Claims 12-16 have been withdrawn from consideration. Claims 1-11 stand rejected.

Claims 2 and 9 are canceled by the present Amendment. New claims 17-21 have been added. Claims 1-11 are currently amended. Claims 1 and 6 have been amended to clarify the language used in those claims. Support for the Amendment to claims 1, 3, and 6 and for new claims 17-21 can be found in the specification on page 15, line 13 to page 16, line 12 and in Example 1. Claims 4, 5, 10, and 11 have been amended to correct the antecedent basis for those claims. Claims 3-5, 7, 8, 10, and 11 have been amended to make the language of those claims consistent with that used in the other claims.

No new matter has been added by the present Amendment. Applicant specifically reserves the right to pursue the subject matter of the canceled or amended claims in a related application. The present Amendment is introduced for the sole purpose of furthering prosecution. Applicant respectfully requests reexamination and reconsideration of the case in light of the present Amendments and the following remarks. Each of the rejections levied in the Office Action is addressed individually below.

Rejection under 35 U.S.C. § 102(b) for alleged lack of novelty

Claims 1-3 and 6-9 stand rejected under 35 U.S.C. § 102(b) on the ground that they are anticipated by Lee *et al.* (1996, *Proc. Natl. Acad. Sci., USA*, 93:6043-47). The Examiner states that Lee teaches methods for identifying a compound that is responsible for demethylation of PP2A, and therefore, Lee anticipates the claims. Applicant respectfully disagrees.

As amended, independent claims 1 and 3 require steps of “providing a plurality of test agents.” Lee does *not* describe or suggest such a step.

Independent claim 6 describes a method in which effects are assessed in an assay that includes PP2A *and* a PP2A methylase enzyme, a PP2A demethylase enzyme, or both. Lee does not describe such an assay. Lee describes an assay in which PP2A is contacted with fractions thought to contain a PP2A demethylase enzyme. Through this assay, PP2A methylesterase was identified. By contrast, the present claims recite contacting a composition with an assay that *already contains* both PP2A and either a PP2A methylase enzyme or a PP2A demethylase enzyme (or both). Lee does not describe such an assay.

Still further, certain dependent claims (e.g., claims 17, 20, and 21) specify that test agents or compositions are identified that affect *activity* of a PP2A methylase or PP2A demethylase enzyme. Identification of the enzyme itself, as described in Lee, does not identify agents or compositions that *affect activity* of the enzyme.

Yet further, amended claim 3 and new claim 19 describe methods for identifying agents and/or compositions that modulate the phosphorylation status of a phosphorylated protein. Lee does *not* describe or suggest such a step.

In order to anticipate, a reference must teach *every element* of the claimed invention. Lee does not teach all of the steps recited in the pending claims. Applicant, therefore, respectfully submits that Lee does not anticipate the present claims and respectfully requests that the rejection be removed.

Rejection under 35 U.S.C. § 103(a) as allegedly being obvious

Claims 4, 5, 10, and 11 stand rejected under 35 U.S.C. § 103(a) on the ground that they are unpatentable over Lee *et al.* in view of Roder *et al.* (U.S. Patent 6,541,468). The Examiner states that it would have been obvious to one of ordinary skill in the art to modulate PP2A activity by demethylating the enzyme, as taught by Lee, in order to reduce hyperphosphorylation of tau, because Roder teaches the relationship between PP2A activity and pathological tau hyperphosphorylation. Applicant respectfully disagrees.

The deficiencies of Lee are described in the section above, are not remedied by the teachings of Roder. Roder teaches a method for treating Alzheimer's disease and other disorders characterized by tau hyperphosphorylation using indolocarbazole derivatives. The assays presented in Roder are *not* methods for identifying modulators of PP2A methylation. Instead, the assays presented in Roder test the ability of *individual* indolocarbazole derivatives to inhibit specific protein *kinases* (*i.e.*, ERK2 and cdc2). Clearly, kinases are *not* phosphatases. Applicant submits, therefore, that the assays described in Roder do not involve testing a *plurality of candidate test agents and/or compositions* for their ability to modulate the methylation status of a *phosphatase* (*e.g.*, PP2A), as recited in the present claims. These teachings do not remedy the deficiencies of Lee.

Moreover, although Roder mentions that it would be "therapeutically desirable" to identify agents that modulate tau phosphorylation, and that the "most convincing cellular

models” regarding tau hyperphosphorylation involve PP2A inhibition, Roder does not mention or even *hint* that tau phosphorylation could be decreased by modulating PP2A methylation. Indeed, the present specification provides, *for the very first time*, the surprising discovery that modulating PP2A methylation has an effect on the phosphorylation status of phosphorylated proteins (*e.g.*, tau). Prior to the present specification, one of ordinary skill in the art would not have expected that screening for agents that modulate PP2A methylation would identify agents that modulate phosphorylation status of phosphorylated proteins, such as tau. This is a significant and surprising contribution to the art.

Applicant submits that Lee and Roder, together or in combination, do not render obvious the present claims. Applicant, therefore, respectfully requests that the rejection be removed.

Rejection under 35 U.S.C. § 112 for alleged lack of enablement

Claims 1-11 stand rejected under 35 U.S.C. § 112 for alleged lack of enablement. The Examiner states that the specification does not provide enablement for “altering a protein activity,” “a protein activity,” or “a phosphorylated protein.” While not agreeing with the Examiner, and solely in order to further prosecution, Applicant has amended the claims to remove recitation of “altering a protein activity” and “a protein activity.” The presently amended claims recite methods for identifying agents and/or compositions that modulate *PP2A methylation status* or that modulate *phosphorylation status* of a phosphorylated protein whose phosphorylation status is regulated by PP2A, not agents that alter a “protein activity.” Applicant, therefore, respectfully submits that the rejection as it relates to recitation of these terms is rendered moot by the present Amendment.

With respect to recitation of “a phosphorylated protein,” the Examiner states that one of ordinary skill in the art would have to perform “undue experimentation to determine which . . . protein would work in the present invention.” Applicant disagrees and respectfully submits that the specification is fully enabling for recitation of “a phosphorylated protein.” The level of skill in the art of protein phosphorylation is high. Protein phosphorylation has been extensively studied for over 70 years, and numerous methods for assaying protein phosphorylation were readily available in the art at the time when the application was filed. Thus, only routine experimentation is required to determine whether a given protein is phosphorylated or not. Thousands (if not millions) of phosphorylated proteins have already been identified, and any

phosphorylated protein could be utilized in the methods recited by the present claims in order to identify agents and/or compositions that modulate the phosphorylation status of that protein. Applicant, therefore, respectfully submits that the specification is fully enabling for recitation of “a phosphorylated protein.” Applicant, therefore, respectfully requests that the rejection be removed.

Rejection under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite

Claims 1-11 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner states that the independent claims are incomplete because they are directed to identifying a compound, but lack any such steps. Applicant has amended independent claims 1 and 6 to recite steps. Applicant, therefore, respectfully requests that the rejection be removed.

The Examiner further states that the terms “an extract of a natural product” and “an extract of a traditional medicine” in claims 7 and 8 are “meaningless and read on water to air.” Applicant respectfully disagrees and submits that the fact that the terms recited in the present claims could encompass water or air does not render them meaningless. The present claims are drawn to screening methods, and *any* extract of a natural product or extract of traditional medicine could be utilized in the screening methods recited by the present claims. The purpose of such claims is to identify new functional characteristics of such extracts that were not previously known to exist. Although one might predict that water or air would be unlikely to affect PP2A methylation or phosphoprotein phosphorylation, one cannot know this *for certain* without first performing the screening method recited in the present claims. As the screening methods can be performed utilizing *any* extract of a natural product or extract of a traditional medicine, recitation of these terms is *not* meaningless and is *not* indefinite. Applicant respectfully requests that the rejection be removed.

The Examiner further states that the title of the invention is not descriptive and that a new title is required that is clearly indicative of the invention to which the claims are directed. While not agreeing with the Examiner, and solely in order to further prosecution, Applicant has

amended the title of the invention to “Systems and Methods for Identifying Modulators of Protein Methylation and Phosphoprotein Phosphatase.” Applicant respectfully submits that this title is clearly indicative of the invention to which the present claims are directed. Applicant, therefore, respectfully requests that the rejection be removed.

Conclusion

For all of the reasons set forth above, each of the rejections in this case should be removed and the application should proceed to allowance. A Notice to that effect is respectfully requested.

If, at any time, it appears that a phone discussion would be helpful, the undersigned would greatly appreciate the opportunity to discuss such issues at the Examiner’s convenience. The undersigned can be contacted at (617) 248-5175.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,

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